International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 25-07-2019; Accepted: 27-08-2019
www.medicalsciencejournal.com
Volume 5; Issue 10; October 2019; Page No. 128-133

Clinical Assessment of the Dysfunctional Uterine Bleeding in Female Patients in Bihar Region

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Abstract
DUB can occur during lifespan of a woman at any time from menarche, occasionally even after the menopause in ovulatory and anovulatory cycles. This condition has enormous consequences with regard to social life, morbidity, and clinical load. DUB can be classified into primary, secondary and iatrogenic groups. Primary DUB is due to dysfunction arising in the hypothalamopitutary-ovarian axis or dysfunction in the endometrium itself. Secondary DUB is due to endocrinopathies, hematological, vascular disease, liver disorders. Iatrogenic DUB is caused by drugs, exogenous hormone administration, and intrauterine contraceptive devices. So DUB is a diagnosis of exclusion; and one should proceed through logical stepwise evaluation to rule out all other causes of abnormal uterine bleeding. Management of DUB is not complete without tissue diagnosis especially in per menopause and postmenopause. It has been known to be associated with almost any type of endometrium, even apparently normal endometrium like proliferative and secretory type. Some other histology of endometrium in DUB are irregular ripening, irregular shedding, atrophy, hyperplasia and carcinoma. Many a times the clinical and intra operative diagnosis does not correlate with histopathological diagnosis. Hence the present study was planned for clinical assessment of the dysfunctional uterine bleeding in female patients in Bihar region.
The present study was planned in Department of Obstetrics and Gynaecology, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India. Total 25 cases of the patients attending the Gynaecological outpatient department with dysfunctional uterine bleeding complete history was taken with regard to age, parity, socioeconomic status, history of bleeding from other sites, pattern of menstrual irregularity i.e. age at menarche, type, duration, amount of blood loss and associated pain, any other gynaecological co-morbidity, previous hormone treatment if any and any previous endocrine problem. Medical illness and pelvic pathology were ruled out clinically. Pap smear was done.
The data generated from the present study concludes that histopathological study of endometrium in females with abnormal uterine bleeding plays an important role in diagnosing various histological patterns and aetiopathological factors. Hence histopathological examination is mandatory, in cases of peri-menopausal and postmenopausal abnormal uterine bleeding.

Keywords: Dysfunctional Uterine Bleeding, DUB, Abnormal Discharge, Endometrium, Bihar, etc

Introduction
Abnormal uterine bleeding (AUB) is one of the most common Gynaecologic presentations which prompt a patient to consult the Gynecological.1 AUB is categorized into two broad groups. First is due to organic causes, having some pathology like fibroid, polyp etc and the second is the so called Dysfunctional uterine bleeding (DUB) when there is absence of organic disease of the genital tract or in other words 'abnormal bleeding from the uterus un-associated with tumor, inflammation or pregnancy. Abnormal uterine bleeding (AUB) is a common problem among (non-pregnant) women in the reproductive age. Formerly, it was known as dysfunctional uterine bleeding (DUB). AUB is responsible for significant health problem and social embarrassment and it is one of the common reasons women seek health care. It has a significant impact on the quality of life for the women. Women with abnormal bleeding have a lower quality of life than the general female population.
The normal length of the menstrual cycle is normally between 24 days and 38days. A normal menstrual period generally lasts up to 8days. Abnormal uterine bleeding (AUB) is bleeding from the uterus that is longer than usual or that occurs at an irregular time. (Bleeding during pregnancy has different causes). AUB leads to loss of productivity and may result in surgical interventions. AUB is reported to occur in 9 to 14% women between menarche and menopause. The prevalence varies in each country. In India, the reported prevalence of AUB is around 17.9%.
The International Federation of Gynaecology and Obstetrics (FIGO) Menstrual Disorders Working Group has proposed to abandon the use of dysfunctional uterine bleeding (DUB), while continue to use the terms abnormal uterine bleeding (AUB) and heavy menstrual bleeding (HMB). HMB includes menometrorrhagia (excessive uterine bleeding during menstrual periods and at irregular intervals), metrorrhagia (bleeding at irregular intervals) and polymenorrhoea (more frequent periods). HMB is defined as "excessive menstrual blood loss which interferes with the woman's physical, emotional, social and material quality of life, and which can occur alone, or in combination with other symptoms.
To standardize nomenclature of AUB, a new system known by the acronym PLAM-COEIN, was introduced in 2011 by FIGO. The PALM-COEIN system is based on etiology and pathology of disorder, where PALM describing structural causes(polyp; adenomyosis; leiomyoma; malignancy and hyperplasia) and COEIN denoting non- structural causes of AUB (coagulopathy; ovulatory disorders; endometrial factors; iatrogenic; and not classified). Abnormal uterine bleeding in women of reproductive age is a manifestation of

any of a number of pathologic disorders.

Abnormal uterine bleeding (formerly, dysfunctional uterine bleeding [DUB]) is irregular uterine bleeding that occurs in the absence of recognizable pelvic pathology, general medical disease, or pregnancy. It reflects a disruption in the normal cyclic pattern of ovulatory hormonal stimulation to the endometrial lining. The bleeding is unpredictable in many ways. It may be excessively heavy or light and may be prolonged, frequent, or random [16]. About 1-2% of women with improperly managed anovulatory bleeding eventually may develop endometrial cancer. AUB should be suspected in patients with unpredictable or episodic heavy or light bleeding despite a normal pelvic examination. Typically, the usual moliminal symptoms that accompany ovulatory cycles will not precede bleeding episodes. Because AUB is considered a diagnosis of exclusion, the presence or absence of signs and symptoms of other causes of anovulatory bleeding must be determined. Patients who report irregular menses since menarche may have polycystic ovarian syndrome (PCOS). PCOS is characterized by anovulation or oligo-ovulation and hyperandrogenism. These patients often present with unpredictable cycles and/or infertility, hirsutism with or without hyperinsulinemia, and obesity.

Abnormal uterine bleeding (AUB) is irregular uterine bleeding that occurs in the absence of pathology or medical illness. It reflects a disruption in the normal cyclic pattern of ovulatory hormonal stimulation to the endometrial lining. The bleeding is unpredictable in many ways. It might be excessively heavy or light, prolonged, frequent, or random. This condition usually is associated with anovulatory menstrual cycles but also can present in patients with oligo-ovulation. AUB occurs without recognizable pelvic pathology, general medical disease, or pregnancy. It is considered a diagnosis of exclusion. AUB is a common diagnosis, making up 5-10% of cases in the outpatient clinic setting. Patients with abnormal uterine bleeding (AUB) have lost cyclic endometrial stimulation that arises from the ovulatory cycle. As a result, these patients have constant, noncycling estrogen levels that stimulate endometrial growth. Proliferation without periodic shedding causes the endometrium to outgrow its blood supply. The tissue breaks down and sloughs from the uterus. Subsequent healing of the endometrium is irregular and dyssynchronous [2].

Chronic stimulation by low levels of estrogen will result in infrequent, light AUB. Chronic stimulation from higher levels of estrogen will lead to episodes of frequent, heavy bleeding. In ovulatory cycles, progesterone production from the corpus luteum converts estrogen primed proliferative endometrium to secretory endometrium, which sloughs predictably in a cyclic fashion if pregnancy does not occur. Heavy but regular uterine bleeding implies ovulatory bleeding and should not be diagnosed as abnormal uterine bleeding (AUB). Subtle disturbances in endometrial tissue mechanisms, other forms of uterine pathology, or systemic causes might be implicated. Anovulatory cycles are associated with a variety of bleeding manifestations. Estrogen withdrawal bleeding and estrogen breakthrough bleeding are the most common spontaneous patterns encountered in clinical practice. Iatrogenically induced anovulatory uterine bleeding might occur during treatment with oral contraceptives, progestin-only preparations, or postmenopausal steroid replacement therapy. Anovulatory cycles have no corpus luteal formation. Progesterone is not produced. The endometrium continues to proliferate under the influence of unopposed estrogen.

Eventually, this out-of-phase endometrium is shed in an irregular manner that might be prolonged and heavy. This pattern is known as estrogen breakthrough bleeding and occurs in the absence of estrogen decline. This frequently occurs in women approaching the end of reproductive life. In older women, the mean length of menstrual cycle is shortened significantly due to aberrant follicular recruitment, resulting in a shortened proliferative phase. Ovarian follicles in these women secrete less estradiol. Fluctuating estradiol levels might lead to insufficient endometrial proliferation with irregular menstrual shedding. This bleeding might be experienced as light, irregular spotting. Eventually, the duration of the luteal phase shortens, and, finally, ovulation stops. Dyssynchronous endometrial histology with irregular menstrual shedding and eventual amenorrhea result. Treatment with oral contraceptives, progestin-only preparations, or postmenopausal steroid replacement therapy might be associated with iatrogenically induced uterine bleeding. Progesterone breakthrough bleeding occurs in the presence of an unfavorably high ratio of progestin to estrogen. Intermittent bleeding of variable duration can occur with progestin-only oral contraceptives, depo-medroxyprogesterone, and depo-levonorgestrel. Progesterone withdrawal bleeding can occur if the endometrium initially has been primed with endogenous or exogenous estrogen, exposed to progestin, and then withdrawn from progestin. Such a pattern is seen in cyclic hormonal replacement therapy [3].

The primary defect in the anovulatory bleeding of adolescents is failure to mount an ovulatory luteinizing hormone (LH) surge in response to rising estradiol levels. Failure occurs secondary to delayed maturation of the hypothalamic-pituitary axis. Because a corpus luteum is not formed, progesterone levels remain low. The existing estrogen primed endometrium does not become secretory. Instead, the endometrium continues to proliferate under the influence of unopposed estrogen. Eventually, this out-of-phase endometrium is shed in an irregular manner that might be prolonged and heavy, such as that seen in estrogen breakthrough bleeding.

Anovulatory bleeding in menopausal transition is related to declining ovarian follicular function. Estradiol levels will vary with the quality and state of follicular recruitment and growth. Bleeding might be light or heavy depending on the individual cycle response. An international expert panel including obstetrician/gynecologists and hematologists has issued guidelines to assist physicians in better recognizing bleeding disorders, such as von Willebrand disease, as a cause of menorrhagia and postpartum hemorrhage and to provide disease-specific therapy for the bleeding disorder [2, 17]. Historically, a lack of awareness of underlying bleeding disorders has led to underdiagnosis in women with abnormal reproductive tract bleeding. The panel provided expert consensus recommendations on how to identify, confirm, and manage a bleeding disorder [4, 5].

An underlying bleeding disorder should be considered when a patient has any of the following:

- Menorrhagia since menarche
- Family history of bleeding disorders

Personal history of 1 or more of the following: (1) Notable

bruising without known injury; (2) bleeding of the oral cavity or gastrointestinal tract without obvious lesion; or (3) epistaxis greater than 10 minutes duration (possibly necessitating packing or cautery)

If a bleeding disorder is suspected, consultation with a hematologist is suggested. Abnormal uterine bleeding is a common diagnosis, making up 5-10% of cases in the outpatient clinic setting. Because most cases are associated with anovulatory menstrual cycles, adolescents and perimenopausal women are particularly vulnerable. About 20% of affected individuals are in the adolescent age group, and 50% of affected individuals are aged 40-50 years. In a study of 400 perimenopausal women, the most common type of bleeding pattern was menorrhagia (67.5%), and the most common pathology was simple endometrial hyperplasia without atypia (31%).

Patients who experience repetitive episodes might experience significant consequences. Frequent uterine bleeding will increase the risk for iron deficiency anemia. Flow can be copious enough to require hospitalization for fluid management, transfusion, or intravenous hormone therapy. Chronic unopposed estrogenic stimulation of the endometrial lining increases the risk of both endometrial hyperplasia and endometrial carcinoma. Timely and appropriate management will prevent most of these problems. Many individuals with abnormal uterine bleeding are exposed to unnecessary surgical intervention, such as repeated uterine curettage, endometrial ablative therapy, or hysterectomy, before adequate workup and a trial of medical therapy can be completed [6].

Iron deficiency anemia: Persistent menstrual disturbances might lead to chronic iron loss in up to 30% of cases. Adolescents might be particularly vulnerable. Up to 20% of patients in this age group presenting with menorrhagia might have a disorder of hemostasis. Endometrial adenocarcinoma: About 1-2% of women with improperly managed anovulatory bleeding eventually might develop endometrial cancer [7].

Infertility associated with chronic anovulation, with or without excess androgen production, is frequently seen in these patients. Patients with polycystic ovarian syndrome, obesity, chronic hypertension, and insulin-resistant diabetes mellitus particularly are at risk. The goals of therapy for abnormal uterine bleeding (AUB) are to control and prevent recurrent bleeding, correct or treat any pathology present, and induce ovulation in patients who desire pregnancy. Age, past history, and bleeding amount influence management [8].

After initial treatment and resolution of an episode of AUB, patients need to be educated that most often chronic therapy is mandatory to prevent further episodes. Reassure patients that most bleeding stops with the appropriate hormonal therapy. Explain the physiologic reason for the anovulatory bleeding pattern. This is particularly true for the adolescent patient who establishes a predictable ovulatory type of menstrual pattern over time. Perhaps the best measure of successful treatment is a good menstrual calendar. Encourage patients to keep a calendar to record daily bleeding patterns. This will serve to document severity of blood loss and impact on daily activities. For patient education resources, see Women's Health Center and Pregnancy Center, as well as Vaginal Bleeding, Birth Control Overview, Birth Control Methods, and Pap S mear.

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Methodology

The present study was planned in Department of Obstetrics and Gynaecology, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India. Total 25 cases of the patients attending the Gynaecological outpatient department with dysfunctional uterine bleeding complete history was taken with regard to age, parity, socioeconomic status, history of bleeding from other sites, pattern of menstrual irregularity i.e. age at menarche, type, duration, amount of blood loss and associated pain, any other gynaecological co-morbidity, previous hormone treatment if any and any previous endocrine problem. Medical illness and pelvic pathology were ruled out clinically. Pap smear was done.

After admission laboratory investigations were obtained which includes hemoglobin estimation, platelet count, bleeding time, clotting time, blood grouping and Rh typing, comment on peripheral smear, fasting blood glucose, urine analysis and thyroid function test. Pelvic scan was done.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: Patients having dysfunctional uterine bleeding.

Exclusion Criteria: Patients having any detectable organic pathology like tumor, pregnancy, inflammation, medical disorders like blood dyscrasias, thyroid abnormalities

Results and Discussion

Dysfunctional uterine bleeding is irregular menstrual bleeding that is not caused by a serious condition such as disease or pregnancy complication. It is usually caused by changing hormones level which may affect ovulation. Dysfunctional uterine bleeding is the most common cause of abnormal vaginal bleeding in women reproductive years. It can have a substantial, financial and quality of life burden and affects women health both medically and socially.

There are some risk factors which cause dysfunctional uterine bleeding they are obesity, stress, irregular sleeping pattern, over work, endometriosis, prolonged oestrogen or progesterone use, drugs or alcohol abuse can disrupt normal hormone balance.

Dysfunctional uterine bleeding is abnormal uterine bleeding in the absence of organic cause is the most frequent urgent gynaecological problem of women. Organic etiologic of dysfunctional uterine bleeding include coagulation defects, pathology involving the reproductive tract infections, systematic disease and local lesions must be ruled out first. It usually to secondary to an ovulation. Dysfunctional uterine bleeding is one of the significant problems seen among patients attending gynaecological outpatient department.

Table 1: Age group & No. of Cases

Age (years)	No. of Womens
Below 20 years	2
20 – 30 years	9
31 – 40 years	6
41 – 50 years	4
51 and above years	4
Total	25

Table 2: Parity & No. of Cases

Age (years)	No. of Woman's
Null Parity	1
Parity 1	1
Parity 2	3
Parity 3	7
Grand multipara	13
Total	25

Table 3: Bleeding type with number of patients

Bleeding Type	No. of Woman's
Heavy Menstrual Bleeding	6
Frequent Menstrual Bleeding	4
Heavy or Prolonged Bleeding	3
Intermenstrual Bleeding	4
Infrequent Menstrual Bleeding	5
Postmenopausal bleeding	3
Total	25

Table 4: Endometrial Histopathology observation

Endometrial Histopathology observation	No. of Woman's
Proliferative Endometrium	9
Secretory Phase	6
Endometrial Hyperplasia	4
Menstrual Phase	2
Atrophic Endometrium	3
Endometrial Metaplasia	1
Total	25

Authors have suggested that higher incidence in multipara can be explained on the basis of general clinical population which shows higher incidence of multipara. Israel *et al* also reported that DUB is a disease of multipara [9]. Hamblen observed parity doubtlessly enhances the incidence of irregular bleeding [10]. Joshi *et al* and Rosario *et al* reported 61.6% and 97% of DUB cases were multiparous respectively [11, 12].

In DUB any type of endometrium may be found, even normal endometrium i.e. endometrium consistent with the day of menstrual cycle., Hoon CN *et al* reported proliferative endometrium in 50.85% of women having DUB [13]. Whereas lower incidence of proliferative endometrium was observed by Sanaullah *et al* (31%) [14]. Higher incidence of proliferative phase of endometrium was reported by Somboonporn W *et al* (75%) [15].

The retrospective study of evaluation and histopathological correlation of abnormal uterine bleeding in perimenopausal women was conducted in Bombay. They analysed 112 perimenopausal women was with abnormal uterine bleeding in the age group of 40-52yrs for a period of 6 months. They concluded that 76.1% women were in the age group of 40-45yrs, whereas the incidence was high in parity 3, 28% and grandmultipara 32%, clinically 49% were fibroid uterus, 49 women 43.85% were diagnosed as dysfunctional uterine bleeding [16].

An experimental study was conducted to assess the functional status of thyroid gland in apparently euthyroid women with dysfunctional uterine bleeding. 40 women (euthyroid) with haemorrhagic and no pathologic lesion in the genital tract were compared with 20 women giving normal menstrual cycles as controls. All women underwent thyroid function test. The study concluded that statistically significant differences were observed in value of T.S.H and T3, T4 between both the groups. Proactive was significantly high in haemorrhagic group. Hence sub clinical hyperthyroidism can be potential risk factors for dysfunctional uterine bleeding [17].

A descriptive was study conducted to defect different histopathological findings in abnormal uterine bleeding by conventional dilatation and currettage in department of OBG Unit-Allied Hospital, Faisalabad from December 2002 to March 2005.161 patients underwent diagnostic dilatation and currettage. Maximum patients (59.02%) with abnormal uterine bleeding presented in age group 36-50 years followed by 36.6%and 4.34% in reproductive and adolescent group. They concluded that D and C is a safe and successful procedure for detecting intrauterine patholigic in abnormal uterine bleeding [17].

A descriptive study was conducted to determine the frequency of various types of dysfunctional uterine bleeding and to analyse their findings on endometrial biopsy. In department of OBG in Khyber teaching hospital Peshawar from 1st Jan 2008-31 December 2010.The endometrial biopsy reports bleeding. The study shows that most frequent clinical feature was polymenorrhagia (18%) and metrorrhagia (9%) cases. They concluded the most common presenting complaint of dysfunctional uterine bleeding was polymenorrhagia [18].

A prospectives obeservational single centre study was conducted at Combined Military Hospital Peshawar on 350 women between 35-70 years reporting to Gynaecology department with dysfunctional uterine bleeding. The study shows that approximately 1/3rd of all the gynaecological consultations are related dysfunctional uterine bleeding. This proportion rises to 70% in the peri and postmenopausal years. Majority patients were of age group 35-55 years. Among that 1.47% of patients presented with menorrhagia and 28% C postmenopausal bleeding [19].

A descriptive study was conducted to assess the occurrence of endometrial carcinoma after endometrial resection in women with dysfunctional uterine bleeding in Israel. The study concluded that cases of endometrial carcinoma were diagnosed 3 years after hysterectomy resection of endometrium for dysfunctional uterine bleeding. 2O

A experimental study was conducted to evaluate histopathology of endometrium for identifying the endometrial causes of dysfunctional uterine bleeding in Ramachandan Medical College and Research Institute, Chennai, 620 patients who presented with dysfunctional uterine bleeding. Out of which 40 cases of isolated endometrial lesions diagnosed on histopathology were selected for final analysis. They concluded the most common age group presenting with dysfunctional uterine bleeding was 41-50 years (33.5%).The commonest pattern in these patients was normal cyclic endometrium (28.4%). Other causes identified were complications of pregnancy (22.7%), carcinomas (4.4%), chronic endometritis (4.2%) [20].

DUB is a common gynaecological condition. Diagnosis of DUB is achieved with the combination of the following: history, physical examination, laboratory evaluation, USG and confirmed by endometrial sampling. Dysfunctional uterine bleeding (DUB) is defined as excessively heavy, prolonged, or frequent bleeding of uterine origin that is not due to pregnancy or any recognizable pelvic or systemic cause. Apart from complete history, thorough clinical examination detailed investigations including bleeding time, clotting time, platelet count, prothrombin time, comment on peripheral smear, TSH, FT3 and FT4 to be done to diagnose any medical illness, ultrasonography of pelvis is an added beneficial tool to exclude organic pathology. DUB was most common in perimenopausal age group (41-50 years), majority of them were multipara and most of the cases belonged to middle class family. Though menorrhagia was the most common bleeding pattern almost in all the age group, metrorrhagia, polymenorrhoea and metropahia haemorragica are also not uncommon. In reviewing the histopathologcal study of endometrium, proliferative endometrium is found to be the commonest endometrium pattern (41.88%) followed by hyperplasia (27.5%), secretory (21.88%) etc. Simple hyperplasia was more common than complex and atypical hyperplasia. Proliferative endometrium is the predominantly common in all age groups whereas hyperplastic endometrium mostly seen in the age group of 41- 50 years. The proliferative endometrium was found in patients presenting with menorrhagia, metrorrhagia and haemorragia metropathica. Whereas hyperplastic endometrium was commonly found in patients presenting with menorrhagia.The proliferative, secretory, hyperplastic endometrium was more common in multipara than in primipara and nullipara.

Conclusion

The data generated from the present study concludes that histopathological study of endometrium in females with abnormal uterine bleeding plays an important role in diagnosing various histological patterns and aetiopathological factors. Hence histopathological examination is mandatory, in cases of peri-menopausal and postmenopausal abnormal uterine bleeding.

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